

**REMARKS**

Upon amendment, Claims 124-139 and 141-151 are pending. Claim 140 has been canceled without prejudice. Claim 124 has been amended to recite that the surfactant is degraded after the chemical digestion. Claim 151 has been withdrawn from consideration by the Examiner. Therefore, Claims 124-139 and 141-150 are now under examination.

Particular support for these claims can be found, at least, in original Claims 1, 3-5, 7-9, 11, 13-18, 20-33, 65, 113, 117, and in previously presented Claim 140. *No new matter has been added.*

Amendment and cancellation of the claims herein is not/are not be construed as acquiescence to any of the rejections/objections set forth in the instant Office Action and were done solely to expedite prosecution of the application. Applicants hereby reserve the right to pursue the claims as originally filed or similar claims in this or one or more subsequent patent applications.

**Claim Rejections – 35 U.S.C. § 102(b)*****Claims 124-142, 144-147 and 150 are rejected under 35 U.S.C. §102(a)***

Claims 124-142, 144-147, and 150 are rejected under 35 U.S.C. §102(a) as being anticipated by Zeller et al. Journal of Biomolecular Techniques, 2002, 13(1), 1-4 ("Zeller"). Applicants respectfully disagree and traverse the rejection.

The Examiner alleges that Zeller et al. discloses methods of enhancing trypsin digest (in-gel tryptic digest) of a biomolecule (proteins such as myoglobin) with an acid labile surfactant (ALS) of the instant structure to enhance the MS detection of the proteins.

Applicants respectfully note that Zeller specifically states the sample was processed by first staining "with Coomassie brilliant blue R350 in 10% acetic acid for 2 h and destained overnight in 7.5% acetic acid to ensure total decomposition of ALS." In-gel tryptic digest procedures were then performed. (See top of page 2 of the paper). That is to say, ALS was added to the sample prior to electrophoretic separation, and then ALS was decomposed in the presence of acetic acid prior to tryptic digestion. As such, the *tryptic digestion was performed after the decomposition of ALS.*

As amended, Claim 124 recites a method wherein the surfactant is degraded *after* the chemical digestion. As Zeller only teaches the denaturation of the surfactant *before* the chemical digestion, Zeller can not anticipate the claimed invention.

As such, Applicants respectfully request that the rejections of the claims under 35 U.S.C. § 102(b) should be withdrawn.

### **Claim Rejections – 35 U.S.C. § 103**

#### ***Claims 124-150 are rejected under 35 U.S.C. §103(a)***

Claims 124-150 are rejected under 35 U.S.C. §103(a) as being unpatentable over Lee, *et al.* (WO 00/70334) in view of Zee Yong et al. (Anal. Chem. 2001, 73, 2558-2564) and Nelson (US 6,093,541) *and Meng et al (Anal Chem 2002, 74, 2923-2929; published on the Web 5/9/2002)*. Applicants respectfully disagree and traverse the rejection.

It has been asserted in the Office Action, as it has in prior office actions, that: (1) Lee teaches a method of solubilizing a substance using a surfactant of the invention for various spectroscopic techniques; (2) Zee-Yong et al. teach that it is known to denature a protein before digestion before spectroscopic analysis; and (3) Nelson teaches proteases for use in mass spectrometers.

In this Office Action, the Examiner has included Meng which allegedly establishes that it was known in the art to use acid labile surfactants of the instant structure along with sensitivity enhancements for peptide mapping after in-gel digestion.

Nothing in Lee, alone or in combination with Zee Yong, Nelson and Meng, suggests the instantly claimed method. As described previously, solubilization, a physical change, does not involve the digestion, alkylation or reduction of a molecule (or, as previously argued, any other chemical alteration). As such, it would be understood that there is absolutely no overlap between the prior art and the instantly pending claims.

Nevertheless, Applicants respectfully note that nothing in Lee suggests that the use of the claimed surfactants results in a favorable chemical property in reaction, such as more complete reaction, increased efficiency, increased yield, increased rate, accelerated chemical digestion, or increased utility, as now recited in Claim 1. Nothing in Lee would have lead one of ordinary skill in the art to reasonably expect the enhancement of a chemical property of the alkylation or reduction reaction using these surfactants. That is to say that Lee, at best, might suggest an

increase in solubility of denatured proteins using a surfactant *after the denaturation had already taken place* but would not have suggested an increase in a favorable chemical property of the reaction *during* the denaturation reaction.

Zee-Yong and/or Nelson do not rectify this deficiency as neither suggests the use of a surfactant during the denaturation reaction such that the surfactant use results in a favorable chemical property of the alkylation or reduction reaction.

Similarly, Meng does nothing to rectify the deficiency in Lee. Meng is focused on the analysis by Mass Spectrometry of *intact proteins*. (See, Page 2923, Column 1, 2<sup>nd</sup> sentence). That is to say, nothing in Meng describes the use of an acid-labile surfactant with a denaturation agent such as a protease, CNBr or hydroxylamine. Indeed, the inclusion of such a denaturation agent would prevent the analysis of intact proteins and would thus prevent the characterization of the “diverse set of biological events that produce mass discrepancies between mature proteins and their corresponding open reading frames” which Meng sets out to elucidate. As such, one of ordinary skill in the art would have had no motivation to combine the surfactants of Meng with a denaturation agent during the reaction. As with Lee, at best, Meng might suggest an increase in solubility of intact proteins using a surfactant but would not have suggested an increase in a favorable chemical property of the denaturation of said proteins, let alone the denaturation of said proteins *during* the denaturation reaction.

Thus, the prior art does not teach or suggest all of the claim limitations, nor would there be a reasonable expectation of success in achieving the favorable chemical property based only the physical solubilization of the references cited, alone or in combination. Therefore, Applicants submit that the Office Action has failed to establish a *prima facie* case of obviousness.

Applicants submit that the teachings in Lee et al. (WO 00/70334), whether alone or in combination with Zee-Yong et al. and/or Nelson and/or Meng, do not teach or suggest Applicants' claimed subject matter. As such, Applicants respectfully request that the rejections of the claims under 35 U.S.C. § 103(a) should be withdrawn.

***Obviousness-Type Double-Patenting***

Claims 124-150 are rejected over Claims 1-7, 13-17, and 19 of United States Patent No. 7,229,539. Applicants request that this rejection be held in abeyance until allowance of the instant claims, but for the obviousness-type double-patenting rejection.

**CONCLUSION**

In view of the amendments and remarks made herein, Applicants submit that the application is in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are respectfully requested. If a telephone conference with Applicants' representative would be helpful in expediting prosecution of the application, Applicants invite the Examiner to contact the undersigned at the telephone number indicated below.

Applicants believe that no additional fees are required in connection with this paper other than the fee for the extension of time submitted herewith. Nevertheless, Applicants authorize the Director to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to Deposit Account No. 04-1105, under Order No. 60009(49991).

In view of the above amendment, applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

Electronic signature: /Nicholas J. DiCeglie, Jr./  
Nicholas J. DiCeglie, Jr.

Registration No.: 51,615  
Edwards Angell Palmer & Dodge LLP  
P.O. Box 55874  
Boston, Massachusetts 02205  
(212) 308-4411  
Attorneys/Agents For Applicant

Customer No. 48990